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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/664,421 | 09/16/2003 | Ryan Bremer | 039363-0703 | 3203 |

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| EXAMINER | |
|---|---|
| NASHED, NASHAAT T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1656 | |

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/664,421 | BREMER ET AL. | |
| | Examiner | Art Unit | |
| | Nashaat T. Nashed, Ph. D. | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *19,20 and 120-141* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 120-141* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/30/05 & 3/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS filed 10/4/04*.

The application has been amended as requested in the communication filed April 10, 2006. Accordingly, claims 1-14 and 20-119 have been canceled, and new claims 120-141 have been added.

Applicant's election without traverse of Group II, claims 15-19 and 120-141, in the reply filed on April 10, 2006 is acknowledged.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s). Several sequences are found in the specification, which are not identified by a sequence identification number. See for examples Tables 1-5 contain amino acid sequence, which are not identified with a sequence identification numbers, and two nucleic acid sequences at page 111, paragraph 412 are not accompanied by a sequence identification number. All Tables containing atomic coordinates represent a disclosure of an amino acid sequence, and therefore require a sequence identifier. Applicants' attention is directed, in particular, to 37 CFR 1.821, which states:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Thus, each time any of the phrases PIM-1, PIM-2 or PIM-III appears in the specification or in the claims, it should be accompanied by SEQ ID NO: (see for example see The Table description at page 34, page 98, the first line in paragraph 365, and example 4 at page 100).

Use of the trademarks names have been noted through out this application. See for example HAMPTON SCREEN 1 and HAMPTON SCREEN 2 at page 100, paragraph 370, the unmodified composition of conditions 2, 7, 14, 17 ..... etc should be stated in the specification. Also, see paragraphs, 152, 365, 371, 242, 251, and page 113, the heading to example 14. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

The disclosure is objected to because of the following informalities: Tables 2 and 3 are objected to because they are not clear and the examiner could not read their content. Applicants must replace the Table with legible copies.

Appropriate correction is required.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15-18 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2004/0146942 ('942, Weihe *et al.*).

The '942 document teaches a method of identifying inhibitors for the actions of PIM-1 kinase and PIM-3, kinase. See the abstract and paragraph 17, and claim 1. It teaches that compounds that bind to PIM-1 and PIM-3 have pain-regulating activity. See paragraphs 14-20. Also, it teaches assay methods of identifying the compounds that bind PIM-1 and PIM-3. See examples 2 and 3.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-19, and 120-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over 2004/0146942 ('942, IDS reference: A3, Weihe *et al.*) in view of the state of the art as exemplified by U. S. patent 6,197,495 ('495), 6,465,484 ('484), and WO 01/87887 ('887).

The teaching of the '942 patent are summarized above.

The '495 patent is relied on to demonstrate the state of the art of identifying compounds that bind to the binding site of a protein using commercially available computer and software. See, in particular, columns 14-16.

The '484 teaches several derivatives of formula I of the instant application to be used as inhibitors of tyrosine protein kinase.

The '887 patent document teaches various derivatives of formula II of the instant applications. See, in particular, formula III at page 6. It teaches that the natural product K252a inhibits several classes of protein kinase. Also, it teaches that the X-ray structure of closely related natural product alkaloid, staurosporine, when bound to protein kinases CDK2 and cAPK confirmed that staurosporine acts as competitive inhibitor for the conserved binding site of adenosine triphosphate, which is found in all protein kinases and noted that a large number of natural products related to K252a structure (indocarbazoles) also inhibit various serine-threonine protein kinase. In addition, it teaches that most of these compounds have and desirable neuronal cytoxic effects due to their lack of specificity. See page 6, last paragraph.

The '942 document provides one of ordinary skill in the art with motivation to identify potential inhibitor for PIM-1 and PIM-3 as they teach that inhibitors of PIM-1 and PIM-3 regulate pain. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to develop a method of identifying potential inhibitors for PIM-1 and PIM-3. Thus, it would have been obvious to one of ordinary skill in the art to use a commercially available computer equipped with suitable software packages such as GRAM, DUCK, and AUTODUCK to fit a model structure of a potential inhibitor to the three-dimensional structure of PIM-1 or a model of PIM-3 based on the structure of PIM-1 to identify possible inhibitors for PIM-1 and PIM-3 as taught in the '495 patent. The ordinary skill in the art would have used known kinase inhibitors such as those taught in '484 and '887 patents documents that binds in the ATP binding site of a protein kinase as a starting material and build to specificity element in order to avoid undesired effects (claims 15-19). The only difference between the cited prior above and the claimed invention are the atomic coordinates disclosed in the specification and provide the molecular structure of the PIM-1 kinase. Data, which are fed into known algorithm such as QUANTA whose purpose is to compare or modify those data using series of processing steps, do not impose a change in processing steps and are thus nonfunctional descriptive material. A method used for its known purpose to compare data sets does not become nonobious merely because a new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that has otherwise been obvious. See *In re Gulak*, 703 F2d 1381, 1385 (Fed. Cir. 1983). Atomic coordinate can't render a known method for identifying inhibitors of enzymes (Claims 120-141).

Claims 15-19, and 120-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mochizuki *et al.* (IDS reference: A187, J. Biol. Chem. 1999, 274, 18659-18666) in view of the state of the art as exemplified by U. S. patent 6,197,495 ('495), 6,465,484 ('484), and WO 01/87887 ('887).

Mochizuki *et al.* teach that the *pim-1* oncogene encodes a serine/threonine kinase (PIM-1) involved in the transduction of cytokine-triggered mitogenic signal, and that PIM-1 is unique in that it is closely cooperates with c-Myc not only in oncogenisis, but also in apoptosis induction. See the abstract. They further teach that PIM-1 may contribute to transformation by inhibiting apoptosis. See page 18659, right column, the last third of the first paragraph.

The '495 patent is relied on to demonstrate the state of the art of identifying compounds that bind to the binding site of a protein using commercially available computer and software. See, in particular, columns 14-16.

The '484 teaches several derivatives of formula I of the instant application to be used as inhibitors of tyrosine protein kinase.

The '887 patent document teaches various derivatives of formula II of the instant applications. See, in particular, formula III at page 6. It teaches that the natural product K252a inhibits several classes of protein kinase. Also, it teaches that the X-ray structure of closely related natural product alkaloid, staurosporine, when bound to protein kinases CDK2 and cAPK confirmed that staurosporine acts as competitive inhibitor for the conserved binding site of adenosine triphosphate, which is found in all protein kinases and noted that a large number of natural products related to K252a structure (indocarbazoles) also inhibit various serine-threonine protein kinase. In addition, it teaches that most of these compounds have and desirable neuronal cytoxic effects due to their lack of specificity. See page 6, last paragraph.

Mochizuki *et al.* provides one of ordinary skill in the art with motivation to identify potential inhibitor for PIM-1 as they teach PIM-1 contributes to transformation by inhibiting apoptosis. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to develop a method of identifying potential inhibitors for PIM-1. Thus, it would have been obvious to one of ordinary skill in the art to use a commercially available computer equipped with suitable software packages such as GRAM, DUCK, and AUTODUCK to fit a model structure of a potential inhibitor to the three-dimensional structure of PIM-1 to identify possible inhibitors for PIM-1 and PIM-3 as taught in the '495 patent. The ordinary skill in the art would have used known kinase inhibitors such as formula II and I taught in '484 and '887 patents documents that binds in the ATP binding site of a protein kinase as a starting material and build to specificity element in order to avoid undesired effects (claims 15-19). The only difference between the cited prior above and the claimed invention are the atomic coordinates disclosed in the specification and provide the molecular structure of the PIM-1 kinase. Data, which are fed into known algorithm such as QUANTA whose purpose is to compare or modify those data using series of processing steps, do not impose a change in processing steps and are thus nonfunctional descriptive material. A method used for its known purpose to compare data sets does not become nonobious merely because a new data becomes available for analysis. Nonfunctional descriptive material cannot render

nonobvious an invention that has otherwise been obvious. See *In re Gulak*, 703 F2d 1381, 1385 (Fed. Cir. 1983). Atomic coordinate can't render a known method for identifying inhibitors of enzymes (Claims 120-141).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen M. Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1656